

PRELIMINARY RESULTS OF HYPERBARIC OXYGEN THERAPY ON PATIENTS ON THE WAITING LIST FOR LIVER TRANSPLANTATION

Resultados iniciais da oxigenoterapia hiperbárica em pacientes em lista de espera para o transplante hepático

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ABSTRACT - Background - Hepatic function is a complex process which involves multiple cellular events. Liver function in cirrhotic patients may be benefited with hyperbaric oxygen therapy. **Aim** - To evaluate clinical and laboratorial data regarding liver function in cirrhotic patients selected for liver transplantation, submitted to hyperbaric oxygen therapy. **Method** - A prospective interventional study was designed, wherein 10 patients were randomized amongst cirrhotic patients selected for liver transplantation. The ages ranged from 20 to 65 years, and all patients presented with a MELD score greater than 15. All patients were submitted to nine sessions of hyperbaric oxygen therapy, on alternated days with the duration of 60 minutes per session, with oxygen atmosphere of 100% and a 2,8 ATM pressure. Dependent parameters included were biochemical and hematologic laboratory values, evaluated before and after hyperbaric oxygen therapy sessions, besides clinical parameters, evaluated considering the Child-Turcotte-Pugh and the MELD scores. Statistical analysis was performed with SPSS (Statistical Package for Social Sciences). **Results** - Three patients (30%) reported decrease in the number and intensity of encephalopathy. There were no cases of spontaneous bacterial peritonitis and gastrointestinal bleeding, and there were no increases on the severity of ascitis. Two patients reported improvement on pruritus, and four improvement on the general status for few weeks following hyperbaric oxygen sessions. **Conclusion** - Hyperbaric oxygen therapy may improve liver function in cirrhosis, and may help to control complications related to liver failure on the preoperative evaluation for liver transplantation.

HEADINGS – Liver transplantation. Oxygen inhalation therapy. Hepatic insufficiency.

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Conflict of interest: none
Financial source: none

Submitted: 07/12/2010
Accepted for publication: 21/12/2010

DESCRITORES - Transplante de fígado. Oxigenoterapia. Insuficiência hepática.

RESUMO - Racional - A função hepática é um processo complexo que envolve múltiplos eventos celulares. Ela, em pacientes cirróticos, pode se beneficiar da terapia com oxigênio hiperbárico. **Objetivo** - Avaliar, de forma preliminar, os dados clínicos e laboratoriais sobre a função hepática em pacientes cirróticos em lista de espera para transplante hepático, submetidos à oxigenoterapia hiperbárica. **Método** - Estudo prospectivo com intervenção, no qual 10 pacientes foram escolhidos aleatoriamente entre os pacientes cirróticos em lista de espera para transplante hepático. A idade variou de 20 a 65 anos, e todos apresentaram escore MELD maior que 15. Todos os pacientes foram submetidos a nove sessões de terapia com oxigênio hiperbárico, em dias alternados com a duração de 60 minutos por sessão, com atmosfera de oxigênio de 100% e pressão de 2,8 ATM. As variáveis dependentes foram os valores laboratoriais bioquímicos e hematológicos, avaliados antes e após sessões de terapia hiperbárica de oxigênio, além de parâmetros clínicos, considerando-se também o Child-Turcotte-Pugh e o MELD. A análise estatística foi realizada com o SPSS (Statistical Package for Social Sciences), e incluiu média com desvio-padrão. **Resultados** - Três pacientes (30%) relataram diminuição no número e intensidade da encefalopatia. Não houve casos de peritonite bacteriana espontânea e sangramento gastrointestinal, e não houve aumento na gravidade da ascite. Dois pacientes relataram melhora no prurido, e quatro melhora no estado geral em poucas semanas após sessões de oxigenoterapia hiperbárica. **Conclusão** - A oxigenoterapia hiperbárica pode melhorar a função hepática na cirrose e ajudar a controlar as complicações relacionadas à insuficiência hepática na avaliação pré-operatória para transplante de fígado.

INTRODUCTION

Liver disease has significant morbidity and mortality and, at an advanced stage, liver transplantation is a form of potentially curative treatment, although it may not be offered to all patients. This aspect make it a public health problem worldwide^{1,2,12,16}.

In Italy, advanced liver diseases promoted 22,000 deaths in 2000, and in this year 1016 transplants were performed. In 2004, 1,416 patients were awaiting liver transplantation, a number significantly lower than the 4,000 new cases diagnosed in the same period¹. In the United States in 2000, the incidence of liver diseases in advanced stages equaled 5,9:100.000 inhabitants, while the mortality rate was 4,5:100.000 inhabitants¹⁷. Data from the National Transplant System in 2003, had 4,287 patients on the waiting list for liver transplantation, with only 637 transplants performed, ie 14.8% of demand. By October 2005, the waiting list included 6834 patients and were performed 454 transplants, 6.6% of need¹³. These data explain the finding that liver transplantation can not be offered to all patients, even fulfilling the basic requirements for being placed on the waiting list. Also indicate the need to search for new treatment options. The liver is the only mammalian organ that can regenerate, promoting hypertrophy and hyperplasia of the remaining healthy tissue. This feature has made to develop studies on the control of cell growth, as treatment of liver failure^{4,11}. Among the noninvasive treatment options, hyperbaric oxygen therapy (OXTN) has been one of the most promising, and from year 1990 very well investigated^{6,8,14,15,18,19}. Oxygen therapy is the inhalation of 100% oxygen at a pressure of two to three atmospheres, in special chambers, so called hyperbaric chambers¹⁸. Hyperbaric oxygen therapy has been used successfully to treat several diseases, acute and chronic, and in some syndromes, and was regulated in Brazil by the Federal Council of Medicine in 1995³. However, in the field of hepatology, there are few studies in the literature involving patients in advanced stage, and in waiting list for liver transplantation. In Brazil, it is estimated that the time between inclusion in the waiting list and transplant is approximately 20 months, range that has excluded the transplant for many patients⁹. An attempt to make the transplant process fairer was performed in 2005 by the Ministry of Health when determined that the priority criteria for this procedure should be the severity of the case, and no the time on waiting list¹³.

The aim of this study was to evaluate, in a preliminary way, the effects hematological, biochemical and clinical aspects before and after sessions of hyperbaric oxygen therapy of patients on the waiting list for liver transplantation.

METHODS

It was conducted a prospective, interventional study at the Department of General Surgery and Liver Transplantation, Hospital das Clínicas, Federal University of Pernambuco (HC-UFPE), which constitutes a referral service for treatment and monitoring of patients with liver disease in advanced stage.

Were included 10 patients with the following characteristics: referred to the Clinic of General Surgery and Liver Transplantation, HC-UFPE, aged between 20 and 65, regardless of gender, enrolled as a receptor on liver transplant waiting list; disease patients liver cirrhosis, MELD score equal to or greater than 15, result of serum alpha-fetoprotein not compatible with liver tumor, liver ultrasound not compatible with liver tumor, and finally, the absence of any diseases that contraindicate hyperbaric oxygen therapy. It was performed in a hyperbaric chamber Multiplace Marno® brand, on alternating days, totaling nine sessions lasting 60 minutes in an atmosphere of 100% oxygen at a pressure of 2.8 atmospheres absolute. The variables analyzed were: biochemical, hematological and clinical tests prior to and after nine sessions OXTN, including: red cell count, hemoglobin, hematocrit, leukocyte absolute and relative trombocitometria, dosages of alanine aminotransferase, aspartate aminotransferase, gamma-glutamyltransferase, alkaline phosphatase, total bilirubin and fractions, creatinine, urea, total protein, albumin, globulin and clotting international normalized ratio (INR). Were observed: the occurrence of ascites, spontaneous bacterial peritonitis, pruritus, encephalopathy and gastrointestinal bleeding, and the calculation of the Child-Turcotte-Pugh⁵ and MELD⁹. The findings pre-intervention were called baseline, while at the end, final. Statistical data were analyzed using the Statistical Package for Social Sciences, presented in the form of frequency distribution tables, calculating the mean and standard deviation. The study was approved by the Ethics Committee on Human Research of the Center for Health Sciences, Federal University of Pernambuco.

RESULTS

Of the 10 patients studied, six (60%) were males and four females, mean age equal to 59.00 ± 1.84 years, ranging from 52 to 66 years. The prognostic and laboratory parameters of patients are listed in Tables 1 and 2. Three (30%) showed a decrease in the number and intensity of episodes of encephalopathy. There were non evidence of spontaneous bacterial peritonitis, gastrointestinal bleeding or change in the degree of ascites. Two (20%) reported mild improvement of the rash. Four (40%) reported feeling of well-being for a few weeks after sessions of hyperbaric oxygen therapy.

TABLE 1 - Average values of alpha-fetoprotein and prognostic index of patients undergoing hyperbaric oxygen therapy

	Basal	Final
Serum alpha-fetoprotein (ng/mL)	6,763 ±1,824	*
Index of Child-Turcotte-Pugh		
A (adds 5 to 6 points)	2	1
B (sum items 7-9)	3	5
C (sum of 10 to 15 points)	5	4
Prognostic index of MELD		
5 – 10	1	-
10 – 15	-	1
15 – 20	9	9

*Measure not held

TABLE 2 - Laboratory parameters of patients undergoing hyperbaric oxygen therapy.

Laboratorial parameters	Basal	Final
Creatinine	0,85±0,05	0,95±0,12
Gamma-glutamyltransferase (GGT) (UL)	98,86±36,86	98,67±22,15
Alkaline phosphatase (U / L)	175,31±52,17	210,67±67,46
Total Protein (g / dL)	6,84±0,20	7,40±0,12
Albumin (g / dL)	2,96±0,14	2,91±0,21
Total bilirubin (mg / dL)	3,77±0,59	2,67±0,40
Hemoglobin	12,59±0,31	12,50±0,35
Hematocrit	36,79±1,14	36,27±0,91
Leukocyte	4374,44±360,88	4100,00±754,98
Trombocitometria (per mm ³ - counter Coer)	112333±19303	93666±112914
INR	1,73±0,07	1,58±0,10

DISCUSSION

Every patient with liver disease whose lifetime is expected to be increased after transplantation, should be subjected to this procedure¹⁰. The poor evolution of the patients on the waiting list encourages researchers in the use of hyperbaric oxygen therapy for patients with advanced-stage liver disease, in order to improve their condition and their quality of life, allowing perhaps his arrival at the transplantation in a good condition. Although some studies emphasize the increased speed of liver regeneration and improvement of liver function in severe situations, including hepatic artery thrombosis after transplantation, no significant alterations were seen¹⁹. Laboratory parameters and prognostic indices showed no significant improvement, contrary to what some authors say about the improvement of levels of some enzymes after use of hyperbaric oxygen therapy^{8,14,15,18}. Also, it was not found here data changing or improving the MELD and the Child significantly. Some of the subjective findings, such as those regarding the improvement in pruritus intensity and frequency of episodes of encephalopathy have been reported. The so-called sense of well-being or improvement reported by few patients and

families, though subjective, draw some attention. It is emphasized the case of a patient with hepato-pulmonary syndrome with improvement of his consciousness level, pressure and oxygen saturation⁷.

Hyperbaric oxygen therapy would be effective in improving quality of life of these patients? Treatment can become a bridge, particularly for patients with hepato-pulmonary syndrome, waiting for liver transplantation? Further research is needed; the findings in this article can stimulate further research to answer these and other questions.

CONCLUSION

Hyperbaric oxygen therapy may improve liver function in cirrhosis and help manage the complications related to liver failure in the preoperative evaluation for liver transplantation.

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